

CLAIMS:

- SUB
DI
- 5
1. An expression vector, wherein the expression region comprises:
a promoter;
an intracellular retention signal sequence encoding region; and
a chemokine encoding gene

wherein said intracellular retention signal sequence and said chemokine encoding gene are expressed from said promoter as a single intrakine transcript.

- 10
2. The expression vector of claim 1, further comprising a gene encoding a secreted chemokine.
- 15
3. The expression vector of claim 2, wherein said gene encoding said secreted chemokine is expressed from an internal ribosome entry site.
4. The expression vector of claim 1, further defined as a retroviral vector.
5. The expression vector of claim 1, wherein said intracellular retention signal sequence is an endoplasmic reticulum retention signal sequence.
- 20
6. The expression vector of claim 5, wherein said endoplasmic reticulum retention signal sequence is a KDEL sequence.
- 25
7. The expression vector of claim 6, wherein said KDEL sequence has the amino acid sequence SEKDEL, SEQ ID NO:6.
8. The expression vector of claim 1, wherein said chemokine gene encodes a chemokine that binds to the C-C chemokine 5 receptor, the C-C chemokine 3 receptor, the C-C chemokine 1 receptor or the CXR4 receptor.
- SUB
C2
9. The expression vector of claim 1, wherein said chemokine gene encodes a chemokine that binds to the C-C chemokine 5 receptor.

10. The expression vector of claim 1, wherein said CC chemokine gene encodes a chemokine that binds to the C-C chemokine 3 receptor.

5 11. The expression vector of claim 1, wherein said CC chemokine gene encodes a chemokine that binds to the C-C chemokine 1 receptor.

12. The expression vector of claim 1, wherein said CXC chemokine gene encodes a chemokine that binds to the CXCR4 receptor.

10 SUB
C2
Const
15 13. The expression vector of claim 2, wherein the encoded chemokine is RANTES, MIP-1 α or SDF.

14. The expression vector of claim 2, wherein said secreted chemokine binds to the chemokine receptor.

15. The expression vector of claim 14, wherein one or more amino acids are deleted from the N-terminus of the encoded chemokine.

20 16. The expression vector of claim 1, wherein said intracellular retention signal sequence directs the expressed protein to the endoplasmic reticulum, Golgi apparatus, a lysosome, an intracellular vesicle or other cellular compartment.

25 17. A method of inhibiting phenotypic expression of a chemokine receptor in a cell, wherein the method comprises blocking cell surface expression of said chemokine receptor.

30 SUB
D2
18. The method of claim 17, further defined as comprising the steps of:
obtaining a vector comprising a nucleic acid segment encoding a promoter, an intracellular retention signal sequence and a chemokine receptor binding polypeptide gene; and transducing said vector into said cell;

SUB
D2
CONT.

wherein said vector expresses said intracellular retention signal sequence and chemokine receptor binding polypeptide gene under the transcriptional control of said promoter to produce a fusion polypeptide when transduced into said cell.

5 19. The method of claim 18, wherein said polypeptide is a chemokine, a chemokine analog, an antibody or a peptide.

20. The method of claim 19, wherein said polypeptide is a chemokine.

10 21. The method of claim 18, wherein said polypeptide is RANTES, MIP-1 α , SDF, HIV gp120 or the V3 region of HIV gp120.

22. The method of claim 20, wherein said chemokine is RANTES, MIP-1 α or SDF.

15 23. A method of inhibiting HIV infection of a cell comprising phenotypic knock-out of an HIV co-receptor in said cell.

SUB
C3

20 24. The method of claim 23, wherein said co-receptor is the C-C chemokine 5 receptor, the C-C chemokine 3 receptor, the C-C chemokine 1 receptor or the CXR4 receptor.

25 25. The method of claim 24, further defined as expressing a receptor binding polypeptide fused to an intracellular retention signal sequence in said cell.

26. The method of claim 25, wherein said intracellular retention signal sequence directs the fusion polypeptide to the endoplasmic reticulum, Golgi apparatus, a lysosome, an intracellular vesicle or intracellular organelle.

SUB
A2

30 27. The method of claim 26, wherein said intracellular retention signal sequence is a KDEL sequence.

28. The method of claim 25, wherein said a receptor binding polypeptide is a CC-chemokine, a CXC chemokine, an analog of a CC or CXC chemokine, a single chain antibody, an HIV gp120 protein, a V3 region of HIV gp120 or a peptide that binds to the receptor.

SUB
D37
29. The method of claim 24, wherein said cell is transduced with a CC-chemokine gene fused to an endoplasmic reticulum (ER)-retention signal to intracellularly block the transport and surface expression of an endogenous CC receptor.

10
30. The method of claim 25, wherein said expression is from a viral vector.

31. The method of claim 30, wherein said viral vector is a retroviral vector.

32. The method of claim 23, wherein said cell is a lymphocyte, monocyte, macrophage or a stem cell.

SUB
C4
33. The method of claim 29, wherein said CC receptor is the CCR5, CCR3 or CCR1 receptor.

20
34. The method of claim 24, wherein said cell is transduced with a CXC-chemokine gene fused to an endoplasmic reticulum (ER)-retention signal to intracellularly block the transport and surface expression of an endogenous CXCR4 receptor.

35. A expression vector for treatment of an HIV infection in a subject, wherein said expression vector includes:

25
an expression region which comprises:

a promoter;

an intracellular retention signal sequence encoding region; and

a chemokine encoding gene;

SUB
C5
30
wherein said intracellular retention signal sequence and said chemokine encoding gene are expressed as a single intrakine transcript from said promoter;

SUB
C5
Cont.

and wherein said expression vector is administered to lymphocytes, monocytes, macrophages or stem cells of said subject and wherein said cells exhibit a phenotypic knock out of an HIV co-receptor.

5 36. The expression vector of claim 35, wherein said cells are transduced *ex vivo* with said vector.

37. The expression vector of claim 36, wherein said stem cells are autologous stem cells.

10 38. The expression vector of claim 35, contained in a pharmaceutically acceptable solution.

SUB
C6

15 39. A method of increasing white blood cell count in a subject with an HIV infection comprising administering to said subject a pharmaceutical composition comprising lymphocytes, monocytes, macrophages or stem cells transduced with a vector of claim 1.